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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,388	09/27/2006	Isami Hamamoto	20241/0205420-US0	7913

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DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER
O'DELL, DAVID K

ART UNIT	PAPER NUMBER
1625	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,388	HAMAMOTO ET AL.	
	Examiner	Art Unit	
	David K. O'Dell	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/12/2007 &11/30/2006 & 9/27/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application is a 371 of PCT/JP05/06887 filed 03/30/2005 and claims priority to the following Japanese applications: JAPAN 2004-106668 filed 03/31/2004 and JAPAN 2004-374007 filed 12/24/2004.

Claims 1-13 are pending.

Response to Restriction/Election

2. Applicant's election of group II and the species (the compound of Example 5-116) in the reply filed on February 1, 2008 without traverse is acknowledged. The examiner would like to expand the definition of group II to include the material in previously in group III, in order to expedite prosecution and keep the costs of filing divisional applications down for the applicant. This application contains claims drawn to a nonelected invention with traverse. A complete reply to this action must include a cancellation of nonelected claims or other appropriate action.

The revised group definitions are shown below, Group II is under examination:

Group I, Claims 1-13 drawn to compounds and compositions having a piperidine core (i.e. where in Formula I of claim 1 n is 1 and no other rings are formed by the piperidine ring substituents). If this group is elected, a further election of a single disclosed species of compound is also required. Further restriction based on the election may be made.

Group II, Claims 1-13 drawn to compounds and compositions having an azabicylooctane core (i.e. where in Formula I of claim 1 n is 1 and a carbocyclic ring is formed via a bridging ethyl group that is either R5 and R6 or R3 and R4 taken together). Claims 1-13 drawn to compounds and compositions having an azabicylononane core (i.e. where in Formula I of claim 1 n is 1 and a carbocyclic ring is formed via a bridging propyl group that is either R5 and R6 or R3 and R4 taken together).

Group III, Claims 1-13 drawn to compounds and compositions having a pyrrolidine core (i.e. where in Formula I of claim 1 n is 0 and no other rings are formed by the pyrrolidine ring substituents). If this group is elected, a further election of a single disclosed species of compound is also required. Further restriction based on the election may be made.

Group IV, Claims -13 drawn to compounds and compositions having a core other than that of Groups I-III. If this group is elected, a further election of a single disclosed species of compound is also required. Further restriction based on the election may be made.

Information Disclosure Statement

3. The information disclosure statements filed on November 30, 2006 & September 27, 2006 fail to comply with 37 CFR 1.98(a)(3)(i) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each reference listed that is not in the English language. It has been placed in the application file, but the Japanese language documents referred to therein have not been considered.

See **MPEP 609.01 [R-5]**

(3) For non-English documents that are cited, the following must be provided:

(a) A concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, unless a complete translation is provided; and /or

(b) A written English language translation of a non-English language document, or portion thereof, if it is within the possession, custody or control of, or is readily available to any individual designated in 37 CFR 1.56(c).

Specification

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.

(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Claim Rejections - 35 USC § 112 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain compounds it does not reasonably provide enablement for the scope of compounds bearing the extensive list of substituents. The variables listing "a five or six membered heterocyclic group" should be limited to a small selection of exemplified heterocyclic groups and the phosphorous containing substituents should be removed from the claims.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with

these claims. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to the following:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(A) The breadth of the claims: The claims are very broad encompassing all five or six membered heterocycles, and prophetic phosphorous compounds. **(B) The nature of the invention:** This is a chemical invention requiring the synthesis of compounds and such compounds should have activity as pesticides, acaricides, or insecticides. **(D) The level of one of ordinary skill**: One of ordinary skill is a practicing pesticide scientist or in the case of the compositions a farmer. **(C) The state of the prior art: (E) The level of predictability in the art: (F) The amount of direction provided by the inventor, (G) The existence of working examples, and (H) The quantity of experimentation needed to make or use the invention:** Each one of the factors (**C**, **E-H**) will be discussed in light of the scientific literature when such a factor is being directly pointed to a large capital letter referring to the aforementioned Wands factor will be placed directly after such a remark or explication. The examiner will first consider the Markush structure I of claim 1, and discuss the limitations related to the "how to use requirement" of 112 1st paragraph.

There are a very large number of compound examples (more than a thousand) that were apparently synthesized in the specification included in Tables 2-7, 10-14 (although none of the

compounds in tables 10-14 were characterized of evaluated for biological activity) **(F & G)**. The compounds are relatively homogenous with respect to the substituents on R^2 and the piperidine ring, and the variability is primarily found on the substituent R1, which comes from a phenol starting material. Such phenols are widely available, however the main issue here is the how to use requirement of 112 1st paragraph. The sole information provided on these materials is found on page 168-171, which contains statements with regard to the ability of some of the compounds to kill mites and army worms **(F & G)**. In general the claims are reasonably well defined on R^1 and other variables and given the large number of what appear to be examples the examiner will not take issue with all these groups, however the following definitions are unacceptable based on the state of the art:

~~a heterocyclic group (~~a five or six membered heterocyclic group having at least one hetero atom selected from an oxygen atom, a nitrogen atom, and a sulfur atom[[)]], which may be substituted by G^4, or any one of substituents represented by the following formula:

$-OP(O)(OR^8)SR^9$

Only four examples of heterocycles are shown. Structural requirements for activity as miticides or insecticides are stringent. It is simply not possible that all of the optional substituted heterocycles will meet such requirements. As evidence of the structural requirements for insecticidal activity the examiner submits the following teachings that testify to the state of the art:

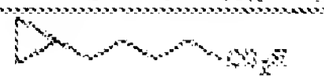
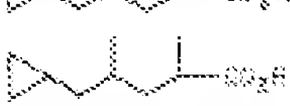
"Four parts of the basic structure have been varied in the synthesis effort: R, X, the carbamate nitrogen substitution, and, in a few cases, the a-methylene group. The effects of some of these variations on the biological activity will be discussed. When X is methylthio, extending the chain length of R (Table 11) results in a moderately active aphicide with the n-propyl compound 3, but

little other results of interest. Branching at the α carbon has a more dramatic effect with maximum activity given by the fully branched compound. The marked effect of small changes in molecular dimensions in this series may be seen with the l-methylcyclopropylcompound 8 which is much less active than the tert-butyl analogue 5. Branching at the p carbon has little beneficial effect (6). One of the substituents on the a carbon can be extended beyond methyl with only moderate loss in contact activity, although systemic activity is sharply lowered as the chain is lengthened (9 and 10)." Thomas A. Magee "Insecticidal Substituted 2-Butanone O-(Methylaminocarbony1)oximes" *Journal of Agricultural and Food Chemistry* **1977**, *25*, 1376-1382.

"Seemingly subtle changes in the structure of compounds in this oxathia series cause substantial changes in biological activity in a pattern analogous to that observed for the previously reported dithia series" Kurtz, et. al. "Novel Insecticidal Oxathiolane and Oxathiane Oxime Carbamates" *Journal of Agricultural and Food Chemistry* **1987**, *35*, 106-114.

Henrick et. al. "Ovicidal Activity and Its Relation to Chemical Structure for the Two-spotted Spider Mite (Tetranychus urticae Koch) in a New Class of Miticides Containing the Cyclopropyl Group" *Journal of Agricultural and Food Chemistry* **1976**, *24*, 1023-1029, show that the simple replacement of a hydrogen atom with a methyl group results in compounds with no activity (compare compound **173** to **175**), "In dodecyl5-cyclopropylpentanoate (**144**), substituting the 2 position or the 3 position of the carboxylate group with a methyl group (**173** and **174**, respectively, Table M) does not affect the ovicidal activity (however, substituting the 2 position of the 7-cyclopropylheptanoate **146** (Figure 1) with a methyl group does considerably lower the activity). The 2,4-dimethyl analogue **176** has much lower activity and the **2,2-dimethyl analogue 175 is inactive** (LCM> 0.1%).

Table IX. Ovicidal Activity of Some Cyclopropylalkyl Esters, Acids, and Alcohols against *T. urticae*

No.	Compound [R = $(CH_2)_nCH_3$]	LC_{90}, % concn
144[a]		0.0029
173		0.0035
174		0.0060
175		>0.10
176		0.036
177	$HO_2C(CH_2)_6C_3H_5$[b]	0.043
178	$HO_2C(CH_2)_7C_3H_5$	0.0056
179	$HO_2CCH(CH_3)(CH_2)_7C_3H_5$	0.031
180	$HO_2C(CH_2)_8C_3H_5$	0.0034
181	$HO_2C(CH_2)_9C_3H_5$	0.030
182	$HO_2C(CH_2)_{10}C_3H_5$	0.0038
183	$HO_2C(CH_2)_{11}C_3H_5$	0.028
184	$HO_2C(CH_2)_{12}C_3H_5$	>0.10
185	$HO_2C(CH_2)_{13}C_3H_5$	>0.10
186	$HO(CH_2)_6C_3H_5$	>0.10
187	$HO(CH_2)_7C_3H_5$	0.034
188	$HO(CH_2)_8C_3H_5$	0.012
189	$HO(CH_2)_9C_3H_5$	0.0086
190	$HO(CH_2)_{10}C_3H_5$	0.021
191	$HO(CH_2)_{11}C_3H_5$	>0.10

[a] Henrick and Staal, 1975d. [b] C_3H_5 = cyclopropyl.

Dekeyser et. al. "Synthesis and Miticidal and Insecticidal Activities of 4- (2 -Fluor oet hyl) - 5,6 -dihydro - 4H- 1,3,4 – oxadiazines" *Journal of Agricultural and Food Chemistry* **1993**, *41*, 1329-1331.

"The presence of one or more halogen atoms in the phenyl moiety of these compounds tends to increase the miticidal and insecticidal activities. However, when a methyl or nitro group is present in the phenyl moiety of these compounds, activities are substantially reduced, **as** in **IIb,h.** Overall, halophenyl compounds **IId-f,j** showed the greatest ovicidal activities against both two spotted spider mites and tobacco budworms, with halophenyl compound **IIf** showing greater activity than either commercial standard."

It is clear that the acaracidic activity of these compounds depends upon the structure of the compound. Indeed it is not possible to predict what the profile of these compounds with diverse heterocycles would be. While authors above have data for the compounds in order to see which compounds are actually active, the applicant has provided little for the scope claimed. In the instant case the claims are not commensurate in scope with the disclosure. We have been

given almost no information in regard to the molecular determinants of insecticidal activity for the compounds of the instant case. **(F & G).** In addition the claims are drawn to "pest control agent". The term pest is broad and would presumably cover weeds, rodents, viruses, bacteria and other flora and fauna not born out by the specification, See Jack R. Plimmer, Derek W. Gammon, Nancy N. Ragsdale "pesticide" in ENCYCLOPEDIA OF AGROCHEMICALS VOLUMES 1-3, Wiley: Hoboken, 2003 pg. 1199:

"Pesticide is a generic term, which is used to refer to many classes of biocidal and nonbiocidal agents. The term includes substances intended for use as plant growth regulators, desiccants, defoliants, etc. Individual classes are frequently characterized by reference to the target organism, e.g., herbicides, insecticides, fungicides, rodenticides, etc. See Active Ingredient. A pesticide is any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest. **Pests can be insects, mice and other animals, unwanted plants (weeds), fungi, or microorganisms such as bacteria and viruses.** Under United States law, a pesticide is also any substance or mixture of substances intended for use as a plant regulator, defoliant, or desiccant (USEPA)."

The factors outlined in *In Re Wands* mentioned above apply here, and in particular as per the MPEP 2164.01 (a): "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

Citation of Relevant Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The following U.S. patents deal with azabicyclononanes and azabicyclooctanes and their application to the pesticide art: 5,859,024; 5,922,732; 5,935,953; 6,174,894; 6,177,442. The applications do not teach or suggest the compounds of the instant case, but can be considered the closest prior art.

Conclusion

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David K. O'Dell whose telephone number is (571)272-9071. The examiner can normally be reached on Mon-Fri 7:30 A.M.-5:00 P.M EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Primary examiner, Rita Desai can be reached on (571)272-0684. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D.K.O.

/Rita J. Desai/
Primary Examiner, Art Unit 1625